

PTO/SB/06a (08-08)

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Form 1449A/PTO

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 12 Attorney Docket Number 24519.6.8402

Complete if Known

Application Number	10/669,162
Filing Date	September 22, 2003
First Named Inventor	Ronald R. Breaker, et al.
Art Unit	1635
Examiner Name	Zara, Jane J.

## U.S. PATENT DOCUMENTS

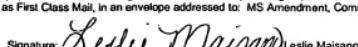
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Column, Lines, Where Relevant Passages Or Relevant Figures Appear
/J/	AA*	US-4,868,116	09-19-1989	Morgan et al.	
	AB*	US-4,980,286	12-25-1990	Morgan et al.	
	AC*	US-5,563,037	10-08-1996	Sutherland et al.	
	AD*	US-3,687,808	08-29-1972	Menigan, Jr. et al.	
	AE*	US-4,845,205	07-04-1988	Huynh Dinh et al.	
	AF*	US-5,130,302	07-14-1992	Spielvogel et al.	
	AG*	US-5,134,066	07-28-1992	Rogers et al.	
	AH*	US-5,175,273	12-29-1992	Bischofberger et al.	
	AI*	US-5,367,066	11-22-1994	Urdea et al.	
	AJ*	US-5,432,272	07-11-1995	Benner et al.	
	AK*	US-5,457,187	10-10-1995	Gmeiner et al.	
	AL*	US-5,459,255	10-17-1995	Cook et al.	
	AM*	US-5,484,908	01-16-1996	Froehler et al.	
	AN*	US-5,502,177	03-26-1996	Matteucci et al.	
	AO*	US-5,525,711	06-11-1996	Hawkins et al.	
	AP*	US-5,552,540	09-03-1996	Haralambidis et al.	
	AQ*	US-5,587,469	12-24-1996	Cook et al.	
↓	AR*	US-5,594,121	01-14-1997	Froehler et al.	
	AS*	US-5,596,091	01-21-1997	Switzer	

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code-Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Column, Lines, Where Relevant Passages Or Relevant Figures Appear	T#
/J/	BA	EP-0070685-B1	01-26-1983			
	BB	WO-9002806	03-22-1990			
	BC	WO-8907136	08-10-1989			
	BD	WO-9717471	05-15-1997			
↓	BE	WO-9717076	05-15-1997			
	BF	WO-0427035	04-01-2004			

Examiner Signature /Jane Zara/ Date Considered 05/18/2009

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Sheet 2 of 12 Attorney Docket Number 24519.6.8402

**U.S. PATENT DOCUMENTS**

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JZ/	AT*	US-5,614,617	03-25-1997	Cook et al.	
	AU*	US-5,681,941	10-28-1997	Cook et al.	
	AV*	US-4,981,957	01-01-1991	Lebleu et al.	
	AW*	US-5,118,800	06-02-1992	Smith et al.	
	AX*	US-5,319,080	06-07-1994	Leumann et al.	
	AY*	US-5,359,044	10-25-1994	Cook et al.	
	AZ*	US-5,393,878	02-28-1995	Leumann et al.	
	Aa1*	US-5,446,137	08-29-1995	Maag et al.	
	AB1*	US-5,466,766	11-14-1995	Buhr et al.	
	AC1*	US-5,514,785	05-07-1996	Van Ness et al.	
	AD1*	US-5,519,134	05-21-1996	Acevedo et al.	
	AE1*	US-5,567,811	10-22-1996	Misura et al.	
	AF1*	US-5,576,427	11-19-1996	Cook et al.	
	AG1*	US-5,591,722	01-07-1997	Montgomery et al.	
	AH1*	US-5,597,909	01-28-1997	Urdea et al.	
	AI1*	US-5,610,300	03-11-1997	Altmann et al.	
	AJ1*	US-5,627,053	05-06-1997	Usman et al.	
	AK1*	US-5,639,873	06-17-1997	Barascut et al.	
	AL1*	US-5,646,265	07-08-1997	McGee	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (# known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T <sup>6</sup>

Examiner Signature	/Jane Zara/	Date Considered	05/18/2009
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Sheet 3 of 12 Attorney Docket Number 24519.6.8402

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/J7/	AM1*	US-5,658,873	08-19-1997	Bertsch-Frank et al.	
	AN1*	US-5,670,633	09-23-1997	Cook et al.	
	AQ1*	US-5,700,920	12-23-1997	Altmann et al.	
	AP1*	US-4,469,863	09-04-1984	Ts'o et al.	
	AQ1*	US-4,476,301	10-09-1984	Imbach et al.	
	AR1*	US-5,023,243	06-11-1991	Tullis	
	AS1*	US-5,177,196	01-05-1993	Meyer, Jr. et al.	
	AT1*	US-5,188,897	02-23-1993	Suhadolnik et al.	
	AU1*	US-5,264,423	11-23-1993	Cohen et al.	
	AV1*	US-5,276,019	01-04-1994	Cohen et al.	
	AW1*	US-5,278,302	01-11-1994	Caruthers et al.	
	AX1*	US-5,286,717	02-15-1994	Cohen et al.	
	AY1*	US-5,321,131	06-14-1994	Agrawal et al.	
	AZ1*	US-5,399,876	03-21-1995	Froehler	
	AA2*	US-5,405,939	04-11-1995	Suhadolnik et al.	
	AB2*	US-5,453,496	09-26-1995	Caruthers et al.	
	AC2*	US-5,455,233	10-03-1995	Spielvogel et al.	
V	AD2*	US-5,466,677	11-14-1995	Baxter et al.	
	AE2*	US-5,476,925	12-19-1995	Letsinger et al.	

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet	4	of	12	Attorney Docket Number	24519.6.8402
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JZ/	AF2*	US-5,519,126	05-21-1996	Hecht	
	AG2*	US-5,536,821	07-16-1996	Agrawal et al.	
	AH2*	US-5,541,306	07-30-1996	Agrawal et al.	
	AP2*	US-5,550,111	08-27-1996	Suhadolnik et al.	
	AJ2*	US-5,563,253	10-08-1996	Agrawal et al.	
	AK2*	US-5,571,799	11-05-1996	Tkachuk et al.	
	AL2*	US-5,587,361	12-24-1996	Cook et al.	
	AM2*	US-5,625,050	04-29-1997	Beaton et al.	
	AN2*	US-5,034,506	07-23-1991	Summerton et al.	
	AO2*	US-5,166,315	11-24-1992	Summerton et al.	
	AP2*	US-5,185,444	02-09-1993	Summerton et al.	
	AQ2*	US-5,214,134	05-25-1993	Weis et al.	
	AR2*	US-5,216,141	06-01-1993	Benner et al.	
	AS2*	US-5,235,033	08-10-1993	Summerton et al.	
	AT2*	US-5,264,562	11-23-1993	Matteucci	
	AU2*	US-5,264,564	11-23-1993	Matteucci	
	AV2*	US-5,405,938	04-11-1995	Summerton et al.	
V	AW2*	US-5,434,257	07-18-1995	Matteucci et al.	
	AX2*	US-5,470,967	11-28-1995	Hui et al.	

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Sheet	5	of	12	Attorney Docket Number	24519.6.8402
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JZ/	AY2*	US-5,489,677	02-06-1996	Sanghvi et al.	
	A22*	US-5,541,307	07-30-1996	Cook et al.	
	AA3*	US-5,581,225	10-01-1996	Maddry et al.	
	AB3*	US-5,596,086	01-21-1997	Matteucci et al.	
	AC3*	US-5,602,240	02-11-1997	De Mesmaeker et al.	
	AD3*	US-5,610,289	03-11-1997	Cook et al.	
	AE3*	US-5,608,046	03-04-1997	Cook et al.	
	AF3*	US-5,618,704	04-08-1997	Sanghvi et al.	
	AG3*	US-5,623,070	04-22-1997	Cook et al.	
	AH3*	US-5,663,312	09-02-1997	Chaturvedula	
V	AI3*	US-5,633,360	05-27-1997	Bischofberger et al.	
	AJ3*	US-5,677,437	10-14-1997	Teng et al.	
	AK3*	US-5,677,439	10-14-1997	Weis et al.	
	AL3*	US-5,539,082	07-23-1996	Nielsen et al.	
	AM3*	US-5,714,331	02-03-1998	Buchardi, deceased et al.	
	AN3*	US-5,719,262	02-17-1998	Buchardi, deceased et al.	
	AO3*	US-60/617,309		Breaker et al.	
	AP3*	US-20050053951	03-10-2005	Breaker et al.	
	AQ3*	US-2007016983	01-18-2007	Muhlbauer	

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(Use as many sheets as necessary)		Filing Date	September 22, 2003
		First Named Inventor	Ronald R. Breaker, et al.
		Art Unit	1635
		Examiner Name	Zara, Jane J.
Sheet	6	of	12
		Attorney Docket Number	
		24519.6.8402	

U.S. PATENT DOCUMENTS

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**FOREIGN PATENT DOCUMENTS**

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Sheet	7	of	12	Attorney Docket Number	24519.6.8402

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>	
/JZ/	CA	Benner et al., Modern metabolism as a palimpsest of the RNA world. PNAS, 86: 7054-7058 (1989)		
	CB	Berkner et al., Abundant expression of polyomavirus middle T antigen and dihydrofolate reductase in an adenovirus recombinant. J. Virology, 61: 1213-1220 (1987)		
	CC	Brown and Burlingham, Penetration of host cell membranes by adenovirus 2. J. Virology, 12: 386-396 (1973)		
	CD	Davidson et al., Overproduction of polyomavirus middle T antigen in mammalian cells through the use of an adenovirus vector. J. Virology, 61: 1226-1239 (1987)		
	CE	Gold et al., From oligonucleotide shapes to genomic SELEX: novel biological regulatory loops. PNAS, 94, 59-64 (1997)		
	CF	Gomez-Foix et al., Adenovirus mediated transfer of the muscle glycogen phosphorylase gene into hepatocytes confers altered regulation of glycogen metabolism. J. Biol. Chem., 267: 25129-25134 (1992)		
	CG	Guo et al., Direct fluorescence analysis of genetic polymorphisms by hybridization with oligonucleotide arrays on glass supports. Nucleic Acids Res., 22: 5456-5465 (1994)		
	CH	Guzman et al., Efficient gene transfer into myocardium by direct injection of adenovirus vectors. Circulation Research, 73: 1201-1207 (1993)		
	CI	Haj-Ahmad et al., Development of a helper-independent human adenovirus vector and its use in the transfer of the herpes simplex virus thymidine kinase gene. J. Virology, 57: 267-274 (1986)		
↓	CJ	Jaeger et al., Improved predictions of secondary structures for RNA. PNAS, 86: 7706-7710 (1989)		

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/JZ CK	Kiga, D., et al., An RNA aptamer to the xanthine/guanine base with a distinctive mode of purine recognition. Nucleic Acids Res. 26: 1755-1760 (1998)				
CL	Laimins, L., et al., Osmotic control of kdp operon expression in Escherichia coli. PNAS, 78: 464-8 (1981)				
CM	Langer et al., Enzymatic synthesis of biotin-labeled polynucleotides: novel nucleic acid affinity probes. PNAS, 78: 6633 (1981)				
CN	Lusky, M.L., et al., Bovine papilloma virus contains an activator of gene expression at the distal end of the early transcription unit. Mol. Cell Bio., 3: 1108 (1983)				
CO	Massie et al., Construction of a helper-free recombinant adenovirus that expresses polyomavirus large T antigen. Mol. Cell. Biol., 6: 2872-2883 (1986)				
CP	Patte, J.C., Biosynthesis of lysine and threonine. In: Escherichia coli and Salmonella: Cellular and Molecular Biology, F.C. Neidhardt, et al., eds, Vol 1, pp 528-541 (1996)				
CQ	Pearson and Lipman, Improved tools for biological sequence comparison. PNAS, 85: 2444 (1988)				
CR	Pease et al., Light-generated oligonucleotide arrays for rapid DNA sequence analysis. PNAS, 91(11): 5022-5026 (1994)				
CS	Ragot et al., Replication-defective recombinant adenovirus expressing the Epstein-Barr virus (EBV) envelope glycoprotein gp340/220 induces protective immunity against EBV-induced lymphomas in the cottontop tamarin. J. Gen. Virology, 74: 501-507 (1993)				
CT	Rodionov, D.A., et al., Comparative genomics of thiamin biosynthesis in prokaryotes. New genes and regulatory mechanisms. Journal of Biological Chemistry, 277: 48949 (2002)				

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				Art Unit	1635
				Examiner Name	J. J. Zara
Sheet	9	of	12	Attorney Docket Number	24519.6.8402

NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.		
/JZ/	CU	Roth, A., Breaker, R.R., Selection in vitro of allosteric ribozymes. In: Methods in Molecular Biology Series - Catalytic Nucleic Acid Protocols (Sioud, M, ed.) Humana, Totowa, NJ (2003)		T <sup>2</sup>
	CV	Seth et al., Role of a low-pH environment in adenovirus enhancement of the toxicity of a Pseudomonas exotoxin-epidermal growth factor conjugate. <i>J. Virol.</i> , 51: 650-655 (1984)		
	CW	Seth et al., Evidence that the penton base of adenovirus is involved in potentiation of toxicity of Pseudomonas exotoxin conjugated to epidermal growth factor. <i>Mol. Cell. Biol.</i> , 4: 1528-1533 (1984)		
	CX	Soukup, G.A., Breaker R.R., Allosteric Ribozymes. In: Ribozymes: biology and Biotechnology. R.K. Gaur and G. Krupp eds. Eaton Publishing (2000)		
	CY	Svensson and Persson, Role of vesicles during adenovirus 2 internalization into HeLa cells. <i>J. Virology</i> , 55: 442-449 (1985)		
	CZ	Tatusov, R.L., et al., The COG database: new developments in phylogenetic classification of proteins from complete genomes. <i>Nucleic Acids Res.</i> , 29: 22-28 (2001)		
	CA1	Usher and McHale, Hydrolytic stability of helical RNA: a selective advantage for the natural 3', 5'-bond. <i>PNAS</i> , 73: 1149-1153 (1976)		
	CB1	Varga et al., Infectious entry pathway of adenovirus type 2. <i>J. Virology</i> , 65: 6061-6070 (1991)		
	CC1	Mandal et al. "A Glycine-Dependent Riboswitch That Uses Cooperative Binding to Control Gene Expression". <i>Science</i> 08 October 2004, Vol. 306, pages 275-279.		
▼	CD1	Vitreschak et al., "Riboswitches: the oldest mechanism for the regulation of gene expression?", <i>Trends in Genetics</i> , January 2004, Vol. 20, No. 1, pages 44-50.		

Examiner Signature	/Jane Zara/	Date Considered	05/18/2009
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Substitute for form 1449/PTO				<i>Complete if Known</i>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> <i>(Use as many sheets as necessary)</i>				Application Number	10/669,162
Sheet	10	of	12	Filing Date	September 22, 2003
				First Named Inventor	Ronald R. Breaker
				Art Unit	1635
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/JZ/	CE1	Tucker et al., "Riboswitches as versatile gene control elements", current Opinion in Structural Biology, 2005, Vol. 15, pages 342-348.			
	CH1	Winkler and Breaker, Genetic control by metabolite-binding riboswitches. Chem BioChem 4(10): 1024-32 (2003)			
	CI1	Nahvi et al., Genetic control by a metabolite binding mRNA. Chem Biol vol 9, page 1043 (2002)			
	CJ1	Winkler et al., Control of gene expression by a natural metabolite-responsive ribozyme. Nature 428(6980): 281-6 (2004)			
	CK1	Antson et al., The structure of trp RNA-binding attenuation protein. Nature vol 374, page 693 (1995)			
	CL1	Barrick et al., New RNA motifs suggest an expanded scope for riboswitches in bacterial genetic control. PNAS USA vol 101, page 6421 (2004)			
	CM1	Kikuchi, The glycine cleavage system: composition, reaction mechanism, and physiological significance. Mol Cell Biochem. Vol 1, page 169 (1973).			
V	CN1	Duce et al., The glycine decarboxylase system: a fascinating complex. Trends Plant Sci vol 6, page 167 (2001)			

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/JZ/	C01	Sudarsan et al., An mRNA structure in bacteria that controls gene expression by binding lysine. Genes Dev vol 17, page 2688 (2003).			T <sup>2</sup>
	CP1	Winkler et al., An mRNA structure that controls gene expression by binding S-adenosylmethionine. Nat Struct Biol vol 10, page 701 (2003).			
	CQ1	Mandal and Breaker, Adenine riboswitches and gene activation by disruption of a transcription terminator. Nature Struct Mol Biol vol 11, page 29 (2004).			
	CR1	Nahvi et al., Coenzyme B <sub>12</sub> riboswitches are widespread genetic control elements in prokaryotes. Nucleic Acids Res, vol 32, page 143 (2004).			
	CS1	Yarnell and Roberts, Mechanism of intrinsic transcription termination and antitermination. Science vol 284, page 611 (1999).			
	CT1	Baugh, C., et al., 2.8 Å crystal structure of the malachite green aptamer. J. Mol. Biol. 301: 117-128 (2000)			
	CU1	Fan et al., Molecular recognition in the FMN-RNA aptamer complex. J. Mol. Biol. 258: 480-500 (1996)			
	CV1	Koizumi, M., et al., Allosteric selection of ribozymes that respond to the second messengers cGMP and cAMP. Nature Struct. Biol. 6: 1062-1071 (1999)			
V	CW1	Serganov, A., et al., Structural basis for discriminative regulation of gene expression by adenine- and guanine-sensing mRNAs. Chem. Biol. 11: 1729-1741 (2004)			
	CX1	Batey, R.T. et al., Structure of a natural guanine-responsive riboswitch complexed with the metabolite hypoxanthine. 18:432: 411-415 (2004)			

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/JZ/	CY1	Jenison et al. High resolution molecular discrimination by RNA. <i>Science</i> 263: 1425-1429 (1994)			
	CZ1	Morris et al., Distributed automated docking of flexible ligands to proteins: Parallel applications of Autodock 2.4. <i>Journal of Computer-Aided Molecular Design</i> 10: 293-304 (1996)			
	CA2	Kubodera et al. Thiamine-regulated gene expression of <i>Aspergillus oryzae</i> thiA requires splicing of the intron containing a riboswitch-like domain in the 5'UTR. <i>FEBS Lett</i> 555: 516-520 (2003)			
	CB2	Mattin et al. Understanding alternative splicing: Towards a cellular code. <i>Nature</i> 438: 386-398 (2005)			
	CD2	Klein et al. Structural basis of blmS ribozyme activation by glucosamine-6-phosphate. <i>Science</i> 313: 1752-1756 (2006)			
	CE2	Blount et al. Development and application of a high-throughput assay for GImS riboswitch activators. <i>RNA Biology</i> 3(2): 77-81 (2006)			
V	CF2	24519.6.8402 Prosecution History for application U.S. 11667153 up to 11.28.2007			
	CG2	24519.6.8402 Prosecution History for European application 03781294 up to 05.12.2008			

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